# Teaching a cell new tricks

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## Tuning the cells machinery to increase production

As anyone knows, trying to replace a resource in limited supply is a significant challenge. In the case of fossil fuels, many avenues have been explored. Perhaps the best known is the use of ethanol from corn as a supplement to gasoline. There has been controversy about this approach since corn is a feedstock and competes for use as a biofuel.

Other mechanisms to provide biofuels are under investigation. One approach that has been explored is to utilize algae to produce fatty acids as biofuels. The challenge has been to find ways to maximize the production of the biofuel in existing options. At Los Alamos National Laboratory, one group has been investigating the cellular mechanism that controls fatty acid synthesis. These compounds, called transcription regulators, control fatty acid production by controlling the first step in the process.

This regulator has two regions in the molecule that are critical to its function. The first is a portion of the molecule that binds to DNA near the gene that it regulates. The second part of the molecule, the binding pocket, binds to a molecule involved in the synthesis of the fatty acid. If the second part is bound to the lipid precursor molecule, the transcription regulator won't bind to the DNA. Therefore, the cell's synthesis is controlled as a function of the concentration of the precursor. The more that is present, the less of the regulator that binds to the DNA and the less synthesis occurs.

Knowing this effect of the regulator, the researchers looked at the structure of the complex of the precursor with the regulator. By determining which parts of the regulator are responsible for binding to the precursor, they were able to use that information to guide them in how to make alterations in the regulator to see how it affected the binding of the precursor.

Using a computer program that modeled the binding pocket, they examined the effect of substituting different amino acids for one that is found in the original molecule. The changes in binding are predicted based on interactions of individual atoms in each molecule. The results of these modeling calculations provide valuable information about the process. By manipulating the structure of the binding pocket, one can then affect the binding of the complex to the DNA. Therefore, it is possible to control the synthesis of the fatty acid by changing the interaction at the binding pocket. This finding could be used to optimize fatty acid metabolism in microorganisms used to produce biofuel.

Reference: "Modulation of FadR Binding Capacity for Acyl-CoA Fatty Acids Through Structure-Guided Mutagenesis," The Protein Journal 34 (5), 359 (2015); doi: 10.1007/

s10930-015-9630-1. Authors: John-Paul Bacik, Chris Yeager, Scott Twary, and Ricardo Martí-Arbona (Bioenergy and Biome Sciences, B-11).

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